

SEQUENCE LISTING

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 QIU, XIANYANG
 YEH, PING

<120> CONJUGATES COMPRISING HUMAN IL-18 AND
 SUBSTITUTION MUTANTS THEREOF

<130> PU60053

<140> TO BE ASSIGNED

<141> 2004-04-14

<150> 60/462,947

<151> 2003-04-15

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 157

<212> PRT

<213> Homo sapiens

<400> 1

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5						10					15
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
			20						25					30	
Met	Thr	Asp	Ser	Asp	Cys	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
		35						40					45		
Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile

50		55		60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile				
65		70		75
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys				
	85		90	
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys				
	100		105	
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu				
	115		120	
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu				
	130		135	
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp				
145		150		155

<210> 2

<211> 157

<212> PRT

<213> Mus musculus

<400> 2

Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg Asn Ile Asn				
1		5		10
Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe Glu Asp Met				
	20		25	
Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg Leu Ile Ile				
	35		40	
Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly Leu Ala Val Thr Leu Ser				
	50		55	
Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn Lys Ile Ile				
65		70		75
Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp Ile Gln Ser				
	85		90	
Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn Lys Met Glu				
	100		105	
Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys Gln Lys Glu				
	115		120	
Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu Asn Gly Asp				
	130		135	
Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser				

145

150

155

<210> 3

<211> 203

<212> PRT

<213> Homo sapiens

<400> 3

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Met His His His His His His Thr Arg Gly Met Ala Ala Glu Pro Val
 1           5           10           15
Glu Asp Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr
          20           25           30
Leu Tyr Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe
        35           40           45
Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln
        50           55           60
Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr
65           70           75           80
Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser
          85           90           95
Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val
          100          105          110
Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser
          115          120          125
Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp
          130          135          140
Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln
145           150           155           160
Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu
          165          170          175
Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp
          180          185          190
Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
          195          200

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<210> 4

<211> 157

<212> PRT

<213> Artificial Sequence

<220>

<223> Whereby the Cysteine at position 38 of the human
IL-18 sequence has been replaced with Serine.

<400> 4

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Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1             5             10             15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
      20             25             30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
      35             40             45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
      50             55             60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
      65             70             75             80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
      85             90             95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
      100            105            110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
      115            120            125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
      130            135            140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
      145            150            155
```

<210> 5

<211> 157

<212> PRT

<213> Artificial Sequence

<220>

<223> Whereby the Cysteine at position 38 of the human
IL-18 sequence has been replaced with Serine, the
Cysteine at position 68 has been replaced with
Aspartic acid, and the Asparagine at position 78
has been replaced with Cysteine.

<400> 5

```
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1           5           10           15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
          20           25           30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
          35           40           45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
          50           55           60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65           70           75           80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
          85           90           95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
          100          105          110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
          115          120          125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
          130          135          140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145           150           155
```

<210> 6

<211> 157

<212> PRT

<213> Artificial Sequence

<220>

<223> Whereby the Cysteine at position 38 of the human
IL-18 sequence has been replaced with Serine, the
Cysteine at position 68 has been replaced with
Aspartic acid, and the Glutamic acid at position
121 has been replaced with Cysteine.

<400> 6

```
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1           5           10           15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
```


	100		105		110										
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
	115		120		125										
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Leu
	130		135		140										
Gly	Asp	Arg	Ser	Ile	Met	Phe	Thr	Val	Gln	Asn	Glu	Cys			
145			150		155										

<210> 9

<211> 157

<212> PRT

<213> Artificial Sequence

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Leucine at position 144 has been replaced with Cysteine.

<400> 9

Tyr	Phe	Gly	Lys	Leu	Glu	Ser	Lys	Leu	Ser	Val	Ile	Arg	Asn	Leu	Asn
1				5				10						15	
Asp	Gln	Val	Leu	Phe	Ile	Asp	Gln	Gly	Asn	Arg	Pro	Leu	Phe	Glu	Asp
			20					25						30	
Met	Thr	Asp	Ser	Asp	Ser	Arg	Asp	Asn	Ala	Pro	Arg	Thr	Ile	Phe	Ile
			35					40						45	
Ile	Ser	Met	Tyr	Lys	Asp	Ser	Gln	Pro	Arg	Gly	Met	Ala	Val	Thr	Ile
			50					55						60	
Ser	Val	Lys	Ser	Glu	Lys	Ile	Ser	Thr	Leu	Ser	Cys	Glu	Asn	Lys	Ile
65						70					75				80
Ile	Ser	Phe	Lys	Glu	Met	Asn	Pro	Pro	Asp	Asn	Ile	Lys	Asp	Thr	Lys
						85					90				95
Ser	Asp	Ile	Ile	Phe	Phe	Gln	Arg	Ser	Val	Pro	Gly	His	Asp	Asn	Lys
						100					105				110
Met	Gln	Phe	Glu	Ser	Ser	Ser	Tyr	Glu	Gly	Tyr	Phe	Leu	Ala	Cys	Glu
Lys	Glu	Arg	Asp	Leu	Phe	Lys	Leu	Ile	Leu	Lys	Lys	Glu	Asp	Glu	Cys
130								135						140	

Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 10

<211> 157

<212> PRT

<213> Artificial Sequence

<220>

<223> Whereby the Cysteine at position 38 of the human
IL-18 sequence has been replaced with Serine, the
Cysteine at position 68 has been replaced with
Serine, and Aspartic acid at position 157 has been
replaced with Cysteine.

<400> 10

Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Ser Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Cys
145 150 155

<210> 11

<211> 4
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 11
Tyr Phe Gly Lys
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<210> 12
<211> 4
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 12
Leu Glu Ser Lys
1

<210> 13
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 13

Leu Ser Val Ile Arg

1 5

<210> 14

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 14

Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu

1 5 10 15

Phe Glu Asp Met Thr Asp Ser Asp Cys Arg

20 25

<210> 15

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 15

Asp Asn Ala Pro Arg

1 5

<210> 16

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 16

Thr Ile Phe Ile Ile Ser Met Tyr Lys

1 5

<210> 17

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 17

Asp Ser Gln Pro Arg

1 5

<210> 18

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 18

Gly Met Ala Val Thr Ile Ser Val Lys

1 5

<210> 19

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 19

Ile Ser Thr Leu Ser Cys Glu Asn Lys

1

5

<210> 20

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 20

Ile Ile Ser Phe Lys

1

5

<210> 21

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 21

Glu Met Asn Pro Pro Asp Asn Ile Lys

1

5

<210> 22

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 22

Ser Asp Ile Ile Phe Phe Gln Arg

1

5

<210> 23

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 23

Ser Val Pro Gly His Asp Asn Lys

1

5

<210> 24

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 24

Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
1 5 10 15
Lys

<210> 25

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 25

Asp Leu Phe Lys
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<210> 26

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 26

Leu Ile Leu Lys

1

<210> 27

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 27

Glu Asp Glu Leu Gly Asp Arg

1

5

<210> 28

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 28

Ser Ile Met Phe Thr Val Gln Asn Glu Asp

1

5

10